

Establishment and characterization of Asian oral cancer cell lines as in vitro models to study a disease prevalent in Asia

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Abstract:

We have established 3 cell lines ORL-48, -115 and -136 from surgically resected specimens obtained from untreated primary human oral squamous cell carcinomas of the oral cavity. The in vitro growth characteristics, epithelial origin, in vitro anchorage independency, human papillomavirus (HPV) infection, microsatellite instability status, karyotype and the status of various cell cycle regulators and gatekeepers of these cell lines were investigated. All 3 cell lines grew as monolayers with doubling times ranging between 26.4 and 40.8 h and were immortal. Karyotyping confirmed that these cell lines were of human origin with multiple random losses and gains of entire chromosomes and regions of chromosomes. Immunohistochemistry staining of cytokeratins confirmed the epithelial origin of these cell lines, and the low degree of anchorage independency expressed by these cell lines suggests non-transformed phenotypes. Genetic analysis identified mutations in the p53 gene in all cell lines and hypermethylation of p16INK4a in ORL-48 and -136. Analysis of MDM2 and EGFR expression indicated MDM2 overexpression in ORL-48 and EGFR overexpression in ORL-136 in comparison to the protein levels in normal oral keratinocytes. Analysis of the BAT-26 polyadenine repeat sequence and MLH-1 and MSH-2 repair enzymes demonstrated that all 3 cell lines were microsatellite stable. The role of HPV in driving carcinogenesis in these tumours was negated by the absence of HPV. Finally, analysis of the tissues from which these cell lines were derived indicated that the cell lines were genetically representative of the tumours, and, therefore, are useful tools in the understanding of the molecular changes associated with oral cancers.

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